Complete Summary

GUIDELINE TITLE

Pretreatment staging of invasive bladder cancer.

BIBLIOGRAPHIC SOURCE(S)

Jafri SZ, Dinan D, Francis IR, Baumgarten DA, Bluth EI, Bush WH Jr., Casalino DD, Curry NS, Israel GM, Kawashima A, Papanicolaou N, Remer EM, Sandler CM, Spring DB, Fulgham P, Expert Panel on Urologic Imaging. Pretreatment staging of invasive bladder cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 8 p. [61 references]

GUIDELINE STATUS

This is the current release of the guideline.

It updates a previous published version: Jafri SZ, Shetty M, Choyke PL, Bluth EI, Bush WH Jr, Casalino DD, Francis IR, Kawashima A, Papanicolaou N, Rosenfield AT, Sandler CM, Segal AJ, Tempany C, Resnick MI, Expert Panel on Urologic Imaging. Pretreatment staging of invasive bladder cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 8 p. [51 references]

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 23, 2007, Gadolinium-based Contrast Agents: The addition of a boxed warning and new warnings about the risk of nephrogenic systemic fibrosis (NSF) to the full prescribing information for all gadolinium-based contrast agents (GBCAs).

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Invasive bladder cancer

GUIDELINE CATEGORY

Diagnosis
Evaluation
Screening

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nuclear Medicine
Oncology
Radiation Oncology
Radiology
Urology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of radiologic procedures for pretreatment staging of invasive bladder cancer

TARGET POPULATION

Patients with invasive bladder cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. X-ray
    - Chest
    - Radiographic survey of the whole body
    - Intravenous urography
2. Magnetic resonance imaging (MRI)
    - Abdomen
    - Pelvis
    - Cystography
3. Computed tomography (CT)
    - Urography
    - Abdomen and pelvis with contrast
    - Chest
    - Cystography
    - Virtual cystoscopy
4. Nuclear medicine (NUC), bone scan whole body
5. fluorodeoxyglucose positron emission tomography (FDG-PET), whole body
6. Ultrasound (US), bladder
    - Transabdominal
    - Transrectal
    - Endoluminal and transurethral

MAJOR OUTCOMES CONSIDERED

Utility of radiologic procedures in post-treatment follow-up of prostate cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Pretreatment Staging of Invasive Bladder Cancer

Radiologic Procedure	Rating	Comments	RRL*
X-ray chest	9	Effective screen of site of most common hematogenous metastasis.	Min
CT urography	8	Pre- and post-contrast with excretory phase.	Med
MRI pelvis	8	See comments regarding contrast in text under "Anticipated Expectations."	None
X-ray intravenous urography	5		Low
CT abdomen and pelvis with contrast	5	May be appropriate if done in combination with IVU.	High
NUC bone scan whole body	3	Probably not indicated unless bone pain is present.	Med
MRI abdomen	3	Probably not indicated unless CT is inconclusive or in patients with renal failure.	None
CT chest	3	Probably not indicated unless chest radiograph is suspicious.	Med
US bladder transabdominal	3	Limited visualization beyond the bladder wall.	None
FDG-PET whole body	2		High
US bladder transrectal	2		None
CT cystography	2		High
MRI cystography	2		None

Radiologic Procedure	Rating	Comments	RRL*
CT virtual cystoscopy	2		High
X-ray radiographic survey whole body	1		Low
US bladder endoluminal and transurethral	1		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

In 2006, an estimated 61,420 new cases of bladder cancer will occur in the U.S., and 13,600 will die of the disease. The lifetime probability of developing invasive bladder cancer is 1 in 28 for men and 1 in 88 for women in the U.S. Bladder cancer has a high tendency toward multifocality at presentation and at recurrence after treatment. Transitional cell carcinoma of the bladder (TCCB) is the most common cell type, accounting for greater than 90% of all cases of bladder cancer. The average age of patients with TCCB in the U.S. is 65 at diagnosis. Almost 80% of patients with TCCB present with hematuria, which is either gross or microscopic and is usually painless and intermittent.

TCCB spreads by local extension through the basement membrane into the muscular layer, then to the perivesical fat. Progressive extension into the muscular layer allows vascular and lymphatic invasion and more distant spread. The most common sites of hematogenous spread are lung, bone, liver, and brain. Superficial lesions do not metastasize until they invade deeply and may remain indolent for many years. 70% to 85% of TCCB is superficial at presentation, confined to the mucosa or submucosa, without muscle invasion. Only invasive tumors will be considered here. The imaging workup begins after the bladder tumor has been identified cystoscopically and has been proven by biopsy.

TCCB is staged by its extension at presentation and graded I-IV according to microscopic (pathologic) criteria of aggressiveness. The standard staging systems for bladder cancer are the Jewett Strong Marshall (JSM) system and the Tumor Node Metastasis (TNM) system. In the classic JSM staging system, stage A tumors are confined to the lamina propria, while stage B involves the muscularis propria. Stage B is divided into superficial and deep infiltration of the muscularis. Extension of tumor beyond the serosa is stage C, and stage D is characterized by involvement of regional then distant nodes or other organ involvement. The division of stage B into superficial and deep is based on Jewett's observation of an 80% 5-year survival rate for patients with B1 lesions compared with 8% for

patients with B2 lesions in a small series. The TNM system, which is now being used more commonly, encompasses the status of the primary tumor (T), the lymph nodes (N), and any metastasis (M) (see Appendix I in the original guideline document).

Tumor grade relates directly to depth of invasion but inversely to curability, so that the 5-year survival rate of patients with grade III and IV superficial tumors is only half that of patients with low-grade I and II superficial tumors (37% vs. 71%). Patients with invasive tumors with no nodal involvement have a 5-year survival rate of 28%, and those with nodal involvement have a 5-year survival rate of 11%.

Treatment ranges from cystoscopic local excision or segmental bladder resection with pelvic lymphadenectomy for early tumors to irradiation, chemotherapy, and/or radical extirpation for deep invasion. Radical cystectomy with pelvic lymphadenectomy remains the standard treatment for muscle-invasive urothelial tumors of the bladder.

Since clinical staging by cystoscopy and bimanual examination under anesthesia is inaccurate in more than 50% of patients, imaging is vital to the proper treatment of these patients. The principal task is to identify extravesical spread. Unfortunately, none of the imaging modalities can identify microscopic spread to muscle layer, perivesical fat, lymph nodes, or other organs.

Cystography, pelvic angiography, lymphangiography (LAG) with or without percutaneous fine-needle aspiration (FNA) biopsy, and plain-film whole-lung laminography are no longer routinely used in staging TCCB since the advent of cross-sectional imaging.

Plain-Film Skeletal Survey

Because plain-film skeletal survey sensitivity is so low, in the range of 17% to 60%, it is also no longer used. Plain film exam is only useful at a site of increased activity on radionuclide bone scan or local bone pain.

Intravenous Pyelography

Intravenous pyelography (IVP) was once the best screening exam for upper-tract disease and was the most sensitive test in detecting small urothelial lesions. With widespread use of CT urography, the role of IVP in evaluating the renal collecting system and ureter is declining. Although only 60% of known bladder tumors are visualized by IVP, obstruction of a ureteral orifice at the level of the ureterovesical junction is usually due to invasive bladder tumor, if urolithiasis is excluded. Any degree of ureteric obstruction is significantly associated with both decreased overall survival rates and decreased tumor-free interval. Ureteral obstruction can be demonstrated by CT urography.

One group of investigators found synchronous TCC above the bladder in 14 of 597 (2.3%) patients with TCCB, 8 (1.3%) with ureteral TCC, and 6 (1.0%) with renal TCC. They reported a range of incidence of synchronous upper-tract lesions between 0% and 6.4% and stated that IVP "must be performed" when TCCB is

first diagnosed. Retrograde ureteropyelography is also excellent for detailed study of the urothelium, especially when IVP is contraindicated or the results are equivocal. However, recent studies have reported an incidence of 1.1% in which IVP was able to diagnose only 66% of cases.

Chest Radiograph and Computed Tomography

All patients with invasive TCCB need pulmonary evaluation. The chest radiograph is an effective, inexpensive, low-morbidity screen. Patients with equivocal chest radiograph and those thought to be at high risk should have standard chest computed tomography (CT).

Radionuclide Bone Scan

Radionuclide skeletal scintigraphy has a sensitivity ranging from 69% to 100% but is highly nonspecific. Solitary bone lesions in patients with underlying primary malignancies are due to metastases in only 55% of cases. The incidence of bone metastases in bladder cancer patients increases with tumor stage at time of diagnosis, from 5% of patients with early-stage invasive tumors to 15% of patients with locally advanced disease. A 4.6% positive rate was found in 458 bone scan studies. Since therapy was affected in only 0.9%, the conclusion was that scintigraphy has "no place in the routine preoperative staging of bladder carcinoma." Bone scanning may be limited to patients with bone pain and/or elevated levels of serum alkaline phosphatase. Further evaluation with plain films and/or magnetic resonance imaging (MRI) can be helpful, and, if necessary, guided needle biopsy can be definitive.

Ultrasound: Transabdominal, Transrectal, and Transurethral

The distended bladder is a superb acoustic window. Size and location of the tumor affect detectability with ultrasound (US). Lesions smaller than 0.5 cm that are flat and/or near the bladder neck can be easily missed. Nevertheless, detection rates of over 95% are reported. US is limited in visualization beyond the bladder wall and cannot detect nodal enlargement. Also it cannot differentiate wall edema, prominent mural folds, postoperative changes, blood clots, or benign masses. Color Doppler with transrectal ultrasound (TRUS) adds nothing to evaluation of stage or grade.

TRUS is excellent for evaluating prostate and seminal vesicles. Transurethral ultrasound (TUUS) is more sensitive than transabdominal ultrasound (TAUS), and TRUS and is more accurate in staging depth of wall involvement but is not widely available. TRUS provides local staging information with 62% to 100% accuracy, highest for superficial tumors. TRUS staging is unreliable for tumors larger than 3 cm and tumors with calcifications, largely because of acoustic shadowing. It is poor (70%) for evaluating extravesical spread. Three-dimensional US rendering is yet another new diagnostic tool with potential to aid in discriminating superficial from muscle-invasive tumors.

Endoluminal ultrasound (ELUS), also known as intravesical ultrasound (IVUS), uses a miniature, high-frequency transducer introduced by a rigid cystoscope for intravesical evaluation. ELUS is both sensitive and specific in detecting muscle invasion in bladder cancer, with rates comparable to those of TUUS, and it

provides greater bladder wall detail. Limitations include difficulty in depicting the tumor base in certain locations and in depicting the depth of invasion in tumors larger than 2 cm with broad bases.

With progression from TAUS to TRUS to TUUS and ELUS, the diagnostic accuracy of US has improved. In 214 new cases of TCCB with pathological correlation, one study reported overall accuracy of 78.6% in local staging with TAUS. They had 9.8% overstaging and 11.7% understaging. Their accuracy was 87% for stage A, 60.5% for stage B, 41.2% for stage C, and 83.3% for stage D. Another study reported an overall accuracy of 96.5% in diagnosing and staging bladder tumors with TUUS in 104 patients: 96.2% in stage Ta-T1 lesions, 100.0% in T2 lesions, 91.7% in T3 lesions, and 100.0% in T4 lesions. There was no discussion of N or M staging.

Studies have shown ELUS to be 100% sensitive, 75% specific, and 84% accurate in detecting muscle invasion in bladder cancer, with both a positive and negative predictive value of 100%. 3-D rendering had a 66% staging accuracy for pTa tumors, 83% for pT1 tumors, and 100% for >pT1 or muscle invasive tumors.

Computed Tomography of the Pelvis and Abdomen

The primary contribution of conventional CT is distinguishing tumors that are organ-confined from those with extravesical extension. It demonstrates bulky thickening of the bladder wall, perivesical extension, lymph node enlargement, and distant metastases very well. Identification of the primary lesion can be difficult in the areas of the bladder neck and dome. CT cannot distinguish inflammatory postoperative or postradiation edema or fibrosis from tumor and cannot assess depth of invasion of the bladder wall. CT is also unable to detect microscopic or small-volume extravesical tumor extension and metastases in nonenlarged lymph nodes.

One group of investigators found an accuracy of 50% in CT staging of pT2(B1) and pT3a(B2) (*p*=pathologic) lesions, understaging of 29.5% of cases, and overstaging of 20.5% of cases. Staging of pT3b(C) lesions was 46.2% accurate, with 53.8% understaged. Of 16 pT4 lesions, one (6.3%) was correctly diagnosed and 15 were understaged. All had infiltration into prostate or seminal vesicle.

Another study reviewed 437 cases in the literature using CT to stage TCCB. Overall accuracy ranged from 40% to 85%, with correct staging of nodes and metastases ranging from 82% to 97%. For extravesical extension, accuracy ranged from 40% to 92% with a mean of 74%. Another group found overall accuracy of 54.9%, with 39% understaging and 20.7% false negative for extravesical spread. Preoperative CT staging altered planned surgical management in only 3.7% of cases. Multi-detector row helical CT with IV contrast and 60-second delayed images is a highly sensitive and specific method for detecting bladder cancer and associated perivesical invasion, particularly when there is a greater than 7-day time interval between intervention and CT. Its sensitivity and specificity are up to 92% and 98% in this setting, respectively.

Various methods for bladder distension have been studied to increase the accuracy of detecting muscle invasion in bladder cancer on CT imaging. These include evaluating the bladder filled with urine, urine opacified with iodinated

contrast material, and air. These methods have accuracies of approximately 84%, 89% and 93% respectively, with overstaging and understaging percentages comparable, ranging from 4% to 7% for overstaging and 2% to 4% for understaging.

In addition to conventional CT, helical CT with multiplanar reformation (MPR), 3-D reconstruction (3DR), and virtual cystoscopy (CTVC) have also been described in the literature. Using helical CT and MPR, one group of investigators found an overall accuracy of 87.7% in CT staging of all stages of bladder cancer and, more specifically, 76.9% for Ta–T2 lesions and 94.7% for T3–T4 lesions. Pathologic lymph nodes were confirmed in six of seven cases. MPR was shown to be useful in evaluating the origin and extent of extravesical invasion, as well as tumor relationship to the ureter. A study by another group found that the sensitivity of 3DR in detecting bladder carcinomas of all stages was 76.9%. CT cystography and virtual cystoscopy may find use in patients unable to tolerate traditional cystoscopy, in those for whom traditional cystoscopy failed, or in those with narrow-necked bladder diverticula that may contain lesions. Sensitivity for identifying 0.5 mm masses has been reported to be 100%, and for all patients' sensitivities of 95% in detecting neoplasm with an accuracy of 88% have been reported with CT cystography. Virtual cystoscopy provides comparable views to traditional cystoscopy but may not add additional diagnostic data in patients able to tolerate traditional cystoscopy.

Multidetector CT urography provides collecting system opacification comparable to that of IVP.

A recent 200-patient study conducted at a fast-track hematuria clinic demonstrated 93% sensitivity and 99% specificity for bladder cancer detection by CT urography, rates similar to those of traditional cystoscopy. As upper tracts are increasingly evaluated by CT for hematuria, the addition of lower-track evaluation adds negligible cost and avoids the discomfort that may be associated with traditional cystoscopy, thereby streamlining the evaluation of patients with hematuria.

Absolute degree of contrast enhancement of tumor may correlate with histologic grade in bladder transitional cell carcinoma, as demonstrated in a study of 65 patients. Although interesting, this finding may find greater application in research of tumor angiogenesis and regression post antiangiogenesis therapy.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is superior to CT in demonstrating the lower pelvic anatomy. There is striking inherent contrast between the bright perivesical fat and the intermediate-signal-intensity bladder wall on T1-weighted images. Multiplanar imaging and gadolinium enhancement improve visualization of tumors on T1-weighted images. Fat suppression techniques can help identify perivesical extension. Deep-muscle invasion presents as disruption of the low-signal-intensity bladder wall by tumor, which usually is of higher signal intensity. After intravenous gadolinium chelates, TCCB shows earlier and greater enhancement than normal bladder or nonmalignant tissue.

Most recently, one group of investigators demonstrated staging accuracies of 85% and 82% in differentiating superficial from muscle invasive tumors and organ-confined from non-organ-confined tumors, respectively. Additionally, the accuracy of pathologic lymph node detection was 96%. Overstaging occurred in 32% of cases. The length of time elapsed between transurethral resection and MRI did not affect staging accuracy. Another study reviewed 340 cases using MRI. The T staging of tumor was accurate in 73%–96% of cases, and the staging of nodes and metastases was accurate in 73% to 98% of cases. The best staging results were with gadolinium-enhanced T1-weighted fast spin-echo sequences 14 seconds after injection. These authors suggest that following cystoscopic identification of tumor, MRI should be used as the initial imaging modality to stage the tumor. Another group of researchers reviewed 71 patients using gadolinium-enhanced endorectal surface coil and reported an 83% overall staging accuracy. Muscle invasion was diagnosed with 87% accuracy, 91% sensitivity, and 87% specificity. Another study found that MRI performed with ferumoxtran-10 (ultrasmall superparamagnetic iron oxide) contrast demonstrated an accuracy in pathologic lymph node detection of up to 92% and a sensitivity of up to 96%.

As with CT cystography and virtual cystoscopy, there has been interest in MR cystography (including multiplanar reconstructions and virtual cystoscopy) as a replacement for traditional cystoscopy and to assist in staging. High diagnostic accuracy has been demonstrated, with sensitivity of 90.7% and specificity of 94.0% using combined virtual cystoscopy and multiplanar reconstructions. These results are comparable to those of CT, and MR cystography is especially promising in special cases where traditional cystoscopy may be contraindicated (urethral stricture), or suboptimal (narrow-necked bladder diverticula). Similar conclusions were previously drawn by one group of investigators.

Computed Tomography versus Magnetic Resonance Imaging

Noting that MRI appears to have slightly better sensitivity and specificity than CT, one group of researchers felt that its benefits were offset by its increased cost and the length of exam. They limited their use of MRI to equivocal cases. Another group felt that use of CT and MRI may be limited to tumors larger than 5 cm and to solid rather than papillary lesions. Another study stated that MRI and CT have similar accuracy for detecting perivesical fat invasion and that the most notable advantage of MRI is its apparent ability to differentiate between superficial and deep invasion of the bladder wall. Another group concluded that MRI is the best technique for staging invasive tumors, as it was slightly better than or equal to CT at differentiating T3a from T3b lesions and superior to CT for tumors at the bladder dome or base. In deeply infiltrating tumors (stages T3b-T4b), they asserted that MRI "is generally agreed to be the most accurate staging technique," and "when MRI is available, CT is no longer needed." Recently, one investigator in a review article stated that MRI is the investigation of choice for local staging and is the preferred technique in postcystectomy and radiation therapy follow-up. Another group in a review of 143 patients prior to radiotherapy confirmed that MRI is superior to clinical staging and provided additional prognostic information.

Both CT and MRI rely on enlargement of lymph nodes as a criterion for metastasis, but they are limited in detecting metastases to normal-sized nodes. This may change as further studies may corroborate the early results of using

lymphotropic nanoparticle-enhanced MRI for detecting micrometastasis in nonenlarged lymph nodes. Lymph node metastasis in patients with superficial tumors (less than T3) is rare, but if deep muscle layers are involved (T2b) or if extravesical invasion is seen, the incidence of lymph node metastasis rises to 20% to 30% and 50% to 60%, respectively. If a lymph node is considered to contain metastasis, a fine-needle aspiration (FNA) biopsy should be considered. Both CT and MRI are equivalent in their ability to detect nodal enlargement.

Positron Emission Tomography and Radioimmunoscintigraphy

Conventional positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (FDG) is unsuitable for imaging bladder tumors because of its high urinary excretion, although it may have a role in detection of recurrent or metastatic disease. FDG-PET is 67% sensitive, 86% specific, and 80% accurate in detecting pathologic lymph nodes in patients with bladder cancer, which exceeds both CT and MRI. A study correlating FDG-PET and CT results in the same patients reported sensitivity, specificity, and accuracy of 60%, 88%, and 78%, respectively, in nodal and metastasis staging, suggesting improved distant metastatic and locoregional node staging. ^{11}C-choline PET when compared with CT promises slightly increased accuracy of lymph node staging (63.0% vs. 88.9%, $p<0.01$) and may avoid false positive results for lymph nodes due to reactive hyperplasia when compared with CT, although further evaluation with this agent is needed to confirm these findings.

The experimental modality of radioimmunoscintigraphy using anti-MUC1 mucin monoclonal antibody C595 labeled with various radiotracers has been shown to be up to 90% sensitive in detecting invasive cancer and 88% sensitive in detecting distant metastases in sites such as lymph node, bone, and lung.

Recommendations

With the increasingly widespread use of CT urography, the role of IVP is declining. CT urography not only is effective for local staging but also provides concomitant evaluation of the liver as well as nodal status. Chest CT can be limited to those with equivocal chest radiographs. Radionuclide bone scan is not indicated without bone pain and/or elevated serum alkaline phosphatase levels. Plain films can be limited to sites of increased uptake and/or bone pain. US is useful for local tumor (T) staging; TUUS and ELUS appear to be equally effective in this regard. Contrast-enhanced MRI is preferred over CT for local staging and is equivalent in assessing regional lymph nodes. CT or MR virtual cystoscopy may be used in specific cases such as evaluation of narrow-necked bladder diverticula, which may be poorly evaluated by traditional cystoscopy, but they are not indicated in the majority of patients. CT and MR virtual cystoscopic techniques may also be of use in those unable to tolerate traditional cystoscopy and may be considered to streamline evaluation of hematuria, combining staging and screening. MRI of the head is needed only if neurological symptoms are present. PET studies to date are not proven to enhance pretreatment staging and are not indicated until further validation and studies are completed.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF, also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF, a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (e.g., >0.2 mM/kg) and to agents in which the gadolinium is least strongly chelated. The FDA has recently issued a "black box" warning concerning these contrast agents (http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705HCP.pdf). This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m^2), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

Abbreviations

- CT, computed tomography
- FDG-PET, fluorodeoxyglucose positron emission tomography
- IVU, intravenous urography
- Med, medium
- Min, minimal
- MRI, magnetic resonance imaging
- NUC, nuclear medicine
- US, ultrasound

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate selection of radiologic imagine procedures for pretreatment staging of invasive bladder cancer

POTENTIAL HARMS

- The relative radiation level is high for computed tomography (CT) of the abdomen and pelvis with contrast, CT cystography, and CT virtual cystoscopy; medium for CT urography, nuclear medicine (NUC) bone scan of the whole body, and CT of the chest; and low for X-ray intravenous urography and X-ray radiographic survey of the whole body.
- Positron emission tomography (PET) studies to date are not proven to enhance pretreatment staging and are not indicated until further validation and studies are completed.
- Some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed nephrogenic systemic fibrosis, a syndrome that can be fatal. Until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m^2), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Jafri SZ, Dinan D, Francis IR, Baumgarten DA, Bluth EI, Bush WH Jr., Casalino DD, Curry NS, Israel GM, Kawashima A, Papanicolaou N, Remer EM, Sandler CM, Spring DB, Fulgham P, Expert Panel on Urologic Imaging. Pretreatment staging of invasive bladder cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 8 p. [61 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1995 (revised 2007)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Urologic Imaging

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: S. Zafar H. Jafri, MD; David Dinan, MD; Isaac R. Francis, MD; Deborah A. Baumgarten, MD; Edward I. Bluth, MD; William H. Bush, Jr., MDE; David D. Casalino, MD; Nancy S.Curry, MD; Gary M. Israel, MD; Akira Kawashima, MD; Nicholas Papanicolaou, MD; Erick M. Remer, MD; Carl M. Sandler, MD; David B. Spring, MD; Pat Fulgham, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

It updates a previous published version: Jafri SZ, Shetty M, Choyke PL, Bluth EI, Bush WH Jr, Casalino DD, Francis IR, Kawashima A, Papanicolaou N, Rosenfield AT, Sandler CM, Segal AJ, Tempany C, Resnick MI, Expert Panel on Urologic Imaging. Pretreatment staging of invasive bladder cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 8 p. [51 references]

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Relative radiation level information. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 6, 2001. The information was verified by the guideline developer as of June 29, 2001. This summary was updated by ECRI on September 8, 2004. The updated information was verified by the guideline developer on October 8, 2004. This NGC summary was updated by ECRI on February 7, 2006. This summary was updated by ECRI Institute on May 17, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Gadolinium-based contrast agents. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This NGC summary was updated by ECRI Institute on December 3, 2007.

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